Molecular and functional resemblance of differentiated cells derived from isogenic human iPSCs and SCNT-derived ESCs.

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Public Summary:
Patient-specific pluripotent stem cells (PSCs) can be generated via nuclear reprogramming by transcription factors (i.e., induced pluripotent stem cells, iPSCs) or by somatic cell nuclear transfer (SCNT). However, abnormalities and preclinical application of differentiated cells generated by different reprogramming mechanisms have yet to be evaluated. Here we investigated the molecular and functional features, and drug response of cardiomyocytes (PSC-CMs) and endothelial cells (PSC-ECs) derived from genetically relevant sets of human iPSCs, SCNT-derived embryonic stem cells (nt-ESCs), as well as in vitro fertilization embryo-derived ESCs (IVF-ESCs). We found that differentiated cells derived from isogenic iPSCs and nt-ESCs showed comparable lineage gene expression, cellular heterogeneity, physiological properties, and metabolic functions. Genome-wide transcriptome and DNA methylome analysis indicated that iPSC derivatives (iPSC-CMs and iPSC-ECs) were more similar to isogenic nt-ESC counterparts than those derived from IVF-ESCs. Although iPSCs and nt-ESCs shared the same nuclear DNA and yet carried different sources of mitochondrial DNA, CMs derived from iPSC and nt-ESCs could both recapitulate doxorubicin-induced cardiotoxicity and exhibited insignificant differences on reactive oxygen species generation in response to stress condition. We conclude that molecular and functional characteristics of differentiated cells from human PSCs are primarily attributed to the genetic compositions rather than the reprogramming mechanisms (SCNT vs. iPSCs). Therefore, human iPSCs can replace nt-ESCs as alternatives for generating patient-specific differentiated cells for disease modeling and preclinical drug testing.

Scientific Abstract:
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